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# Facile and innovative method for bioglass surface modification: Optimization studies

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ABSTRACT

In this work it is presented a facile and novel method for modification of bioglass surface based on ($Ca_{molten\ salt}^{2+}|Na^{+}_{glass}$) ion exchange by immersion in molten salt bath. This method allows changing selectively the chemical composition of a surface layer of glass, creating a new and more reactive bioglass in a shell that surrounds the unchanged bulk of the original BG45S5 bioglass (core-shell type system). The modified bioglass conserves the non-crystalline structure of BG45S5 bioglass and presents a significant increase of surface reactivity in comparison with BG45S5. Melt-derived bioactive glasses BG45S5 with the nominal composition of 46.1 mol% $SiO_2$, 24.4 mol% $Na_2O$, 26.9 mol% CaO, and 2.6 mol% $P_2O_5$ have been subjected to ion exchange at 480 °C in molten mixture of $Ca(NO_3)_2$ and $NaNO_3$ with molar ratio of 70:30 for different time periods ranging from 0 to 60 min. The optimization studies by using XRF and XRD showed that ion exchange time of 30 min is enough to achieve higher changes on the glass surface without alters its non-crystalline structure. The chemical composition, morphology and structure of BG45S5 and bioglass with modified surface were studied by using several analytical techniques. FTIR and $O_{1s}$ XPS results showed that the modification of glass surface favors the formation of *Si*-$O_{NBO}$ groups at the expense of Si—$O_{BO}$—Si bonds. $^{29}$Si MAS-NMR studies showed that the connectivity of $_{Si}Q^n$ species decreases from cross-linked $_{Si}Q^3$ units to chain-like $_{Si}Q^2$ units and finally to depolymerized $_{Si}Q^1$ and $_{Si}Q^0$ units after ion exchange. This result is consistent with the chemical model based on the enrichment with calcium ions of the bioglass surface such that the excess of positive charges is balanced by depolymerization of silicate network. The pH changes in the early steps of reaction of bioactive glasses BG45S5 and BG45Ca30, in deionized water or solutions buffered with HEPES were investigated. BG45Ca30 bioactive glass exhibited a significant increase in the pH during the early steps of the reaction compared to BG45S5.



## 1. Introduction

The evolution of the biomaterials science over the years experienced a breakthrough in the late 60's, which represented a paradigm shift with the genesis of a new biomaterial class defined as being bioactive [1–4]. The bioactivity was first observed for the bioactive glasses, specifically 45S5 Bioglass® composition, which showed the ability of combine with both soft and hard tissues through the formation of a strong interfacial bond between the glass and the surrounding living tissues by means of the development of an apatite phase [1,2,5–8]. Consequently, bioactive glasses have attracted increasing interest during the past few decades, in particular, in the field of development and study of new glass compositions [1,5], as well as devices potentially suitable for medical purposes, such as bone graft substitute in various clinical applications [9].

The physicochemical reactions occurring at the surface of bioactive glasses have been exhaustively discussed by several articles in recent decades [10–13]. In general, most of the work has been limited to study the ability of certain compositions to form the apatite layer, disregarding an understanding of kinetic factors that can be decisive and highly needed to support further progress in this field.

The reactivity and bioactivity of surface-active glass are commonly described in terms of their composition and connectivity network, i.e., crosslink density of the glass matrix [14]. It is widely recognized that glasses composition containing large amounts of sodium and calcium modifier cations leads to high concentration of nonbridging oxygen (NBO), and thus decreasing the bioglass connectivity network [6,15,16].

Glasses characterized by a highly fragmented network definitely reacts faster in a physiological aqueous environment owing to favorable

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pathways (rich in $Ca^{2+}$ and $Na^{+}$), which allow the water molecule penetrates under the surface, increasing the glass dissolution rate and consequently, the subsequent stages of the glass surface reactions responsible for apatite layer formation. However, the prepare of glassy compositions with low silica content (high content of sodium and calcium) is not interesting from the point of view of bioactivity (silica is a core component of many bioactive materials) [17] and also of stability against devitrification, which exhibit a large tendency to crystallize [18,19]. Furthermore, no other bioactive glass composition has been found to have better biological properties than the 45S5 Bioglass® composition [7].

In this present work, we are proposing the use of surface modification of bioactive glasses based on ($Ca^{2+}_{molten\ salt\ bath}|Na^{+}_{glass}$) ion exchange by immersion in molten salt bath [20], aiming to produce a novel biomaterial with improved surface reactivity in comparison with the original BG45S5 bioglass. In general, the ion exchange method in glass is performed by replacing monovalent alkali ions present in a surface layer of a glass substrate with different ions from a molten salt bath, but less usual for cations with higher valence number (lower ionic mobility within the glassy matrix) [21]. However, ion exchange involving divalent cations or higher valence becomes an attractive method for modifying surface in glasses with high fragmented structure (typical feature of bioglasses). The decision to use calcium as modifier agent was motivated by the dependence of the apatite formation from its concentration and the increased hemostatic activity [22], osteogenic [8,23] and bioglasses reactivity due to the release of $Ca^{2+}$ [24,25].

It is noteworthy that the ion exchange process is restricted to a superficial shell of glass, whereas the chemical composition of the bulk is preserved with its exceptional bioactivity. The proposed method allows a fine control on the rate of apatite layer formation by modulating the ion exchange time, i.e., thickness of the modified surface. Indeed, the thin modified layer of bioglass may act as a "catalyst" for physicochemical reactions (hydration, ion exchange, hydrolysis, polymerization and silica-gel layer formation) occurring at the surface of the bioactive substrate after immersion into physiological aqueous environment as described by Hench's mechanism.

Another feature of ion exchange method is that it allows achieving vitreous compositions that would not be easily prepared without a devitrification by using melt-quenching technique. In addition, it is a very interesting method owing to its low cost, experimental simplicity and high reproducibility [26,27].

Although the ion exchange technique to modify the surface is quite common in glasses industry, its application for bioactive glasses has been limited to silver, aiming bacteriostatic properties [28]. On the other hand, the use of ion exchange aiming to alter the chemical composition and introduce perturbations in the structure of the bioglass surface in order to influence the rate of chemical reactions responsible for biomineralization is novel and it has not yet been explored.

## 2. Material and methods

### 2.1. Preparation of bioglass

Bioglass 45S5 (46.1 mol% $SiO_2$, 26.9 mol% CaO, 24.4 mol% $Na_2O$, and 2.6 mol% $P_2O_5$) was prepared using a traditional melt-quenching technique [18,19]. Monoliths obtained were cut into discs 1 mm thick and 20 mm diameter and polished (diamond paste 6 μm), which were employed in the different characterizations and also in the process of surface modification by the enrichment with calcium ions.

Towards $^{23}Na$ MAS NMR analysis a disc 0.5 mm thick and 20 mm diameter glass block was crushed and reduced to powder with particle sizes below 38 μm. Samples for X-ray powder diffraction (XRD) and differential scanning calorimeter (DSC) were obtained by removing a surface layer of glass monolith by using a variable-speed rotary tool (Dremel MultiPro, Dremel®, Racine, WI, USA) with tungsten carbide drill bits (3 mm tungsten carbide burrs ball, Eternal Tools, Oxfordshire, UK). The glass particles were carefully ground in an agate mortar and sieved in order to select particle size smaller than 38 μm.

### 2.2. Modification of 45S5 surface with calcium ions via ($Ca^{2+}_{molten\ salt\ bath}|Na^{+}_{glass}$) ion exchange

Disc shape samples of the 45S5 were dipped in a molten salt bath of 70% $Ca(NO_3)_2$ and 30% $NaNO_3$ (mol%) prepared in a vertical tubular furnace. A trial and error procedure was used to optimize the bath composition, in order to obtain the highest ratio of $Ca(NO_3)_2/NaNO_3$ (more rich in calcium ions) and at the same time, completely molten at 480 °C [19]. This temperature is high enough to induce the diffusion of ions and below of glass transitions ($T_g = 550$ °C) and onset crystallization temperature ($T_x = 665$ °C) of the 45S5 [29], avoiding any structural modification of the bulk due to heating. In order to standardize the nomenclature for the glassy samples, from now they will receive the following denominations: BG45S5 for the annealed glass and BG45Ca for the specimens with the surface modified with calcium ions.

### 2.3. Effect of immersion time on the glass composition and structure: optimization studies

Five bioglasses polished discs were prepared and dipped in the molten salt bath for several periods: 3, 5, 15, 30 and 60 min. The removal of encrusted salts from the surface of glass disc was carried out through washing cycles in anhydrous ethanol, first in a Soxhlet apparatus for 1 h at the boiling, followed by 15 min in ultrasound bath. For each sample was performed at least 3 cycles to ensure complete removal of salt from the glass surface, and at the end of each cycle the ethanol was exchanged.

Elemental composition of BG45Ca as function of immersion time was determined by X-ray fluorescence using a spectrometer (XRF Shimadzu 1800, Shimadzu Scientific Instruments, Tokyo, Japan). Measurements were carried out directly on the surface of bioglasses discs without any previous preparation. XRF 1800 software was used for quantification of elements oxides. The quantification was carried out by the fundamental parameter (FP) method using the X-ray intensities [30–34].

The structural evolution as a function of ion exchange time was monitored by X-ray diffraction (XRD). XRD diffractograms were collected using a diffractometer (XRD-7000, Shimadzu Scientific Instruments, Tokyo, Japan) with a Bragg Brentano camera geometry, Cu-K incident radiation ($\lambda = 1.5418$ A), 40 kV, 30 mA and acquisition rate of $2° \text{ min}^{-1}$ within the range 10 to 60° (2θ).

### 2.4. Characterization of bioglasses: BG45S5 and BG45Ca30

#### 2.4.1. Atomic force microscopy (AFM)

Topographies of bioglasses discs were obtained using an AFM microscope (Nanosurf EasyScan Flex 2, Nanosurf AG, Liestal, Switzerland), in the intermittent mode, with the tip coated with aluminum (Tap model 190 Al-G, BudgetSensors Innovative Solutions Bulgaria Ltd., Sofia, Bulgaria). The thickness of the Al coating was 30 nm, the resonance frequency was 190 kHz and the stiffness constant was 48 $N \cdot m^{-1}$. Images were recorded in frequency sweep from 0.8 to 1 Hz for a resolution of $512 \times 512$ pixels. The area of analysis used was $10 \times 10\ \mu m^2$.

#### 2.4.2. Elemental analysis of glass: SEM-EDS and 23Na MAS NMR

The concentration profiles were determined by scanning electron microscopy with energy dispersive X-ray spectroscopy (SEM-EDS) line profile analysis in a disc fracture using a scanning electron microscope (JEOL Ltda., JEOL JMS model 6360-Lev, Tokyo, Japan) with an EDS analyzer. In this setup, SEM electron beam is scanned along a preselected line across the sample fracture while X-rays are detected for discrete positions along the line.